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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/505,400	06/22/2005	Stanton L. Gerson	CWR-7784PCT/US	7253

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EXAMINER	
PACKARD, BENJAMIN J	

ART UNIT	PAPER NUMBER
1612	

MAIL DATE	DELIVERY MODE
10/07/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/505,400	GERSON ET AL.	
	Examiner	Art Unit	
	Benjamin Packard	1612	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 July 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *See Continuation Sheet* is/are pending in the application.

4a) Of the above claim(s) *See Continuation Sheet* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *59,60,64,65,75,77,78 and 98* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continuation of Disposition of Claims: Claims pending in the application are 1,59-62,64,65,67,75,77,78,83,85,88,98,101,103-106,111,113,172 and 230-233.
Continuation of Disposition of Claims: Claims withdrawn from consideration are 1,61,62,67,83,85,88,101,103-106,111,113,172 and 230-233.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 07/27/09 has been entered.

Applicants' arguments, filed 07/27/09, have been fully considered. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

LACK OF WRITTEN DESCRIPTION UNDER 35 U.S.C. § 112, FIRST PARAGRAPH:

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 59, 60, 64, 75, 77, and 98 stand rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, specifically rejecting the term "AP endonuclease inhibitors".

Applicants assert the functional language of "AP endonuclease inhibitor with an amine group and binds to the AP site to prevent AP endonuclease-mediated cleavage of phosphodiester bonds" illustrates Applicants were in possession of the claimed genus, given the specification discloses specific AP endonuclease inhibitors, distinguishing characteristics to identify the AP endonuclease inhibitors, and an assay to identify new AP endonuclease inhibitors. Additionally, Applicants assert a *prima facie case* was not satisfied by the Office.

Examiner still disagrees. First, with regards to making a *prima facie case* of lack of written description, while an application as filed is presumed to be have adequate written description, that presumption may be rebutted by reasoning. Here, Applicants assert because a small genus of compounds was disclosed which have the desired effect, that one of skill would recognize Applicants were in possession of the broader genus of AP endonuclease inhibitors. Examiner rebutted this by reasoning there is a lack of core structure which would lead one of skill to know whether a compound was an AP endonuclease inhibitor or not. Further, Examiner cited Rochester for the legal holding that proposed assays are not sufficient to meet written description. While the instant specification differs from Rochester in that some specific inhibitors are disclosed, the generic teaching that the inhibitors must have an amine group is extremely broad, given the number of compounds with an amine group is endless. Where the massive "amine" containing genus is further required to be assayed to determine if the required activity is present produces a fact pattern similar to Rochester. Therefore, as in Rochester, Applicants appear to be trying to claim more than what they were in

possession of at the time of filling, thus encompassing compounds of unknown structure into the claims.

Second, with regards to the specific disclosure, as touched upon above, the disclosure that the compounds must have an amine group is not sufficient, given the endless number of potential compounds which have an amine group. Where Applicants disclose an assay to test for compounds, such disclosure suggests Applicants were not in possession of the claimed compounds, but instead are claiming unknown compounds, with hopes of finding effective compounds through later testing.

Claim Rejections - 35 USC § 112 – Scope of Enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 59, 60, 64, 65, 75, 77, 78, and 98 stand rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling a method of potentiating a therapeutic effect of temozolamide by combination with methoxyamine (MX), does not reasonably provide enablement for treating the broader method of potentiating a therapeutic effect of anticancer agents which induce formation of AP sites by combination with base excision repair inhibitors.

Applicants assert anticancer agents can be used to treat various cancers, where the specific combinations are known in the art. Applicants also discuss the specification as presenting working examples where the BER inhibitors are used to potentiate the

effect of anticancer agents that form AP sties. Applicant also asserts Cramer (US 4,325,950) is not applicable as Terzoudi et al teaches caffeine has been shown to be an inhibitor of ATM/AT, which are key components of DNA damage checkpoint. Further, Applicants cite Seo et al for teaching that caffeine is a base analogue of adenine, which correlates with the extent repair inhibition of DNA double strand breaks.

Examiner disagrees. While one of ordinary skill may know what cancers may be treated by known anti-cancer agents, the instant claims are not limited to the treatment of cancers by their known respective anticancer agents, but instead the claims are directed to administering anticancer agents which induces formation of AP sites, generally, to treat cancers, generally. Thus, one of ordinary skill would be subject to undue experimentation when determining what cancers may be treated by the anticancer agents, given the increased potency of the combination.

With respect to the articles, Examiner first notes the "attached" articles do not appear to have been submitted. Therefore, relying on Applicants interpretation of the same, Examiner notes the disclosure of the prior art appears to be directed to theoretical application, or in vitro application. Again, where the patent cited by Examiner specifically teaches the correlation between in vitro and in vivo testing is unpredictable, the submission of additional in vitro reasoning does not overcome the unpredictability, given in vitro testing is very controlled when compared to the complex in vivo atmosphere.

Claim Rejections - 35 USC § 103

Claims 59, 60, 64, 65, 75, 77, 78 and 98 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fortini et al (Carcinogenesis vol. 13 no. 1 (1992) pp.87-93).

Applicants assert the disclosure does not enable in vivo results, given the instantly amended claims are directed to treating a patient. Additionally, Applicants assert Fortini et al teaches away from administering a BER inhibitor to potentiate the cytotoxicity of an anticancer agent.

Examiner disagrees. First, as discussed in the Final Rejection dated 01/27/09, Fortini et al teaches at pg 91, second paragraph, experiments were done to mimic the in vivo testing by incubating the oligonucleotides with MX and cell extract. The authors note that the in vivo amount of MX had to be increased to produce the same effect. Therefore, not only would the skilled artisan have a reasonable expectation of success when practicing the method of Forini et al in a patient, but it would further be obvious to increase the amount of MX administered to the point that the desired effect occurs, i.e. inhibiting the AP endonucelase activity.

Second, with regard to coadministration, Fortini et al states at pg 91, first paragraph of Discussion, immediately following the section cited by Applicants, "the longer treatment with MX produced an increase in the cytotoxicity of SN2 agents and abolished the protective effect in the case of the Sn1 ones." Thus, the increase of the agent is recognized to have a potentiating effect on cancer agents.

Conclusion

No claims allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Benjamin Packard whose telephone number is 571-270-3440. The examiner can normally be reached on M-F 8-5 EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Frederick Krass can be reached on 571-272-0580. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Benjamin Packard/
Examiner, Art Unit 1612

/Frederick Krass/
Supervisory Patent Examiner, Art Unit 1612